

REMARKS

I. Status of the Claims

Claims 1-18 are pending, and claim 4 has been withdrawn from consideration. No claim has been amended by this response. The Examiner has rejected pending claims 1-3 and 5-18 on the grounds that the claims are drawn to an improper Markush group. Claims 1-3 and 5-18 have been further rejected on the grounds that they are indefinite under § 112, second paragraph. Finally, claims 1-3 and 5-15 have been rejection as obvious under § 103(a) over either Kamber or Urbahns. Applicants would like to thank the Examiner for indicating the elected species of Example 23 was not found in the prior art and expanding his search beyond the elected species. Applicants, however, respectfully traverse each of the rejections in turn.

II. Rejection of Markush Claim

The Examiner has rejected claims 1-3 and 5-18 as being drawn to an improper Markush group, alleging that "the claimed subject matter does not share a substantial structural feature disclosed as being essential to [a common] utility." Office Action at 5. The Examiner further asserts that "the instant Markush Groups possess widely different[] physical and chemical properties." *Id.* Applicants respectfully traverse.

The compounds of claim 1, for example, share a substantial structural feature. This can not be contested. Moreover, Applicants disagree with the Examiner's characterization that the instant Markush Groups possess widely different physical and chemical properties. There is simply no support for this statement in the present application and the Examiner has provided no evidence to support his statement. Applicants' respectfully request that the Examiner, if he is to pursue this argument,

provide some evidence on the record in support of the statements made in the Office Action.

As is discussed in detail below, the Examiner has not established a *prima facie* case of obviousness, and therefore he has not properly asserted any relevant prior art. Because no relevant prior art has as yet been asserted, the Examiner is required to examine the full scope of the claims. Failure to do so is plainly improper. M.P.E.P. § 803.02 ("Following election, the Markush-type claim will be examined fully with respect to the elected species *and further to the extent necessary to determine patentability*. . . . [S]hould no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended.") (emphasis added).

III. § 112, Second Paragraph Rejections

The Examiner made several rejections of claims 1-3 and 5-18 under § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter Applicants regard as the invention. Each of these rejections is traversed below.

A. The Examiner alleges that, in claim 1, claimed variables for R14 and R16 are unclear in that the groups may be "substituted by 1, 2, or 3 substituents chosen from [many groups]," while "[c]hemically, there is no heterocycle with 1 carbon and 1 [nitrogen]." Office Action at 7. Applicants presume the Examiner is referring the following claim language of claim 1, wherein R14 or R16 can be an

. . . N-containing heteroaromatic having 1, 2, 3, 4, 5, 6, 7, 8, or 9 carbon atoms,

where . . . the substituted N-containing heteroaromatic are each independently substituted by 1, 2, or 3 substituents chosen from F, Cl, Br, I, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3,

or 4 carbon atoms, alkoxy having 1, 2, 3, or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

Present Application, Claim 1.

Applicants point out that, as one of ordinary skill in the art would understand, it is the N-containing heteroaromatic and the compounds preceeding it in the claim that are each independently substituted by the 1, 2, or 3 substituents listed. In other words, the 1, 2, or 3 listed substituents relate to the "substituted phenyl, substituted naphthyl, substituted biphenyl, substituted furyl, substituted thienyl and the substituted N-containing heteroaromatic," rather than the R14 and R16 groups alone.

Applicants fail to see how substituting a C₁₋₉ N-containing heteroaromatic with 1, 2, or 3 substituents is indefinite or could be understood as the chemically impossible "heterocycle with 1 carbon and 1 [nitrogen]" as suggested by the Examiner. Office Action at 7. Applicants further respectfully point out that the Examiner is incorrect in noting that a heterocycle must have a minimum of two carbons. *Id.* Indeed, a heterocycle may contain only one carbon if it contains at least two other atoms, such as nitrogen. Therefore, Applicants submit that the present claim is not indefinite as written and request withdrawal of the § 112, second paragraph rejection. If the Examiner persists in making this indefiniteness rejection, Applicants respectfully request further clarification.

B. The Examiner has rejected claims 1-3 and 5-8 as indefinite, alleging that the phrase "a pharmaceutically tolerable salt thereof, in an[y] stereoisomeric form, or a mixture of any such compounds in any ratio" is unclear as claimed. Office Action at 7. The Examiner further suggests amending the claim to recite a "racemic mixture." *Id.*

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Applicants, however, submit that a "racemic mixture" is not the same as "a mixture of any such compounds in any ratio." For example, the claim as presently written refers to a mixture of any of the possible compounds of Formula (I), including a mixture of various pharmaceutically tolerable salts. While racemic mixtures are certainly encompassed within the scope of the present claim, the claim is not so limited.

Furthermore, the Examiner has not shown that the present claim as written is indefinite. In order to meet the requirements of 35 U.S.C. § 112, second paragraph, the claims must define the patentable subject matter with a reasonable degree of particularity and precision. M.P.E.P. § 2173.02. The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. M.P.E.P. § 2173.

In fact, claims 1-3 and 5-8 are clearly and distinctly directed towards any of Formula (I), a pharmaceutically acceptable salt thereof, a stereoisomer of Formula (I), a stereoisomer of a pharmaceutically acceptable salt thereof, or a mixture of any of these compounds. The Examiner has failed to demonstrate, as he must, how this ordinary language is indefinite, but rather merely states in a conclusory fashion that the claims are confusing as written. Therefore, Applicants respectfully request withdrawal of this basis for the § 112, second paragraph rejection for indefiniteness.

C. The Examiner has rejected claim 9 as indefinite, asserting that "[i]t is not very clear as to what applicants want to claim by stating[] 'other pharmacological active compounds.'" Office Action at 7. Again, the Examiner has failed to meet his burden of demonstrating that the scope of the claim is unclear so the public would not be informed

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of the boundaries of what constitutes infringement of the patent. M.P.E.P. § 2173. To the contrary, one of ordinary skill in the art would comprehend with ease the meaning of a “pharmacological active compound” as a compound that exhibits pharmacological activity.

D. The Examiner alleges that claims 16-18 are indefinite for four reasons. First of all, the Examiner states that the claims do not define “[t]he process or step of preparing the pharmaceutical preparation.” Office Action at 8. Applicants, however, respectfully point out to the Examiner that claims 16-18 are composition claims, not process claims. Therefore, as the Examiner knows, Applicants are not required to recite the process for preparing a composition if that process is not the subject of the claims. The word “preparation,” as it is used in the present claims, is a noun and not a verb.

Second of all, the Examiner has asserted that “IKr, IKs, and beta blocker” are not definite.” Office Action at 8. Not only are all of these terms well-understood by those of ordinary skill in the art, but IKr and IKs are also specifically defined in the present specification as a rapidly-activating potassium channel and a slow-activating component, respectfully. Present specification at page 17, ll. 3, 13-14.

Third, the Examiner alleges that the phrase “at least one” is indefinite in that it is open-ended. While Applicants agree that “at least one” is an open-ended phrase, leaving open the possibility of multiple compounds or blockers, this does not in and of itself render the claim indefinite. That a claim is open-ended does not mean, *ipso facto*, that the claim is indefinite or that its scope is unascertainable. To so hold would be to equate the mere breadth of a claim with indefiniteness, a result the M.P.E.P. does not

condone: "Breadth of a claim is not to be equated with indefiniteness. If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph." M.P.E.P. § 2173.04.

Finally, the Examiner has rejected claims 16-18 as indefinite because the phrase "[p]harmaceutically acceptable vehicles and additives [] also do not describe the exact make up of the pharmaceutical preparation." Office Action at 8. Applicants reiterate that the Examiner has failed to meet his burden of demonstrating that the scope of the claim is unclear so the public would not be informed of the boundaries of what constitutes infringement of the patent. M.P.E.P. § 2173. To the contrary, one of ordinary skill in the art would comprehend with ease the meaning of a "pharmaceutically acceptable vehicles and additives" as common and ordinary language in the pharmaceutical arts.

E. Applicants are uncertain whether claims 10-18 have further been rejected under § 112, as the present Office Action does not specifically state any such rejection in Paragraph V of the Office Action. The Examiner appears to refer to portions of § 112, first paragraph in stating that there are "issue[s] of enablement" and "how to use." Office Action at 8-9. If the Examiner is in fact making a rejection, Applicants respectfully request that he do so on the record.

IV. § 103(a) Obviousness Rejections over Kamber and Urbahns

The Examiner has rejected 1-3 and 5-15 under 35 U.S.C. § 103(a) as obvious over Kamber. The Examiner alleges that Kamber teaches "dihydro pyridine

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compounds, compositions and utility for treating cardiovascular disorders.” Office Action at 10. As the Examiner admits, however, Kamber teaches bridges of -CO-NH-CH₂-CO-OR⁷ and -CO-NH-alkyl, whereas the presently claimed compound has a bridge of -CO-NH-CO-O-alkyl. *Id.* Yet the Examiner still concludes that “[o]ne skilled in the art would find ample motivation from prior art(s) to . . . modify the . . . groups” *Id.*

The Examiner further rejected claims 1-3 and 5-15 as obvious over Urbahns. The Examiner alleges that Urbahns teaches “making of substituted 4-phenyl-6-amino-nicotinic acid compounds” Office Action at 11. Again, the Examiner notes the dissimilarity between the reference compound and the present invention, stating that Urbahns “differs from the specific compound by not having the specific bridge,” but still concludes that “one skilled in pharmaceutical art would find ample motivation from prior art(s)” to modify the compound. *Id.*

The Examiner has failed to establish a *prima facie* case of obviousness, and thus Applicants respectfully request withdrawal of this ground for rejection. In order to establish a *prima facie* case, an Examiner must point to, among other things, a suggestion or motivation to modify the reference or to combine reference teachings. M.P.E.P. §2142. The Examiner must set forth “clear and particular” evidence of such motivation, *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) (abrogated on other grounds by *In re Gartside*, 203 F.3d 1305 (Fed. Cir. 2000)), and such a showing must be by “substantial evidence.” *In re Zurko*, 258 F.3d 1378, 1384 (Fed. Cir. 2001).

The Examiner has failed to meet this high burden, and indeed has presented no evidence, much less substantial evidence, that is clear and particular. Instead, the Examiner merely jumps to the premature conclusion that one skilled in the art would be

motivated to modify the references, pointing to no specific suggestion in the references themselves or in the prior art. Rather, the Examiner merely makes the unsupported statement that one would find ample motivation in the prior art. Broad conclusory statements about what the references and the prior art in general teach, standing alone, are not "evidence." In this case, the Examiner has merely summarized the alleged teachings of the references with blanket statements that provide no "clear and particular" evidence of any suggestion or motivation to modify the references. Thus, the Examiner has failed to establish a *prima facie* case of obviousness, and the Applicants respectfully request that this ground for rejection be withdrawn.

V. Conclusion

In view of the foregoing remarks, Applicants respectfully request the reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: July 22, 2003

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